UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,508	03/26/2004	Xing Cheng	26-003820US	8613

7590 09/14/2007

JONES DAY
222 EAST 41ST STREET
NEW YORK, NY 10017

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
09/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/811,508	CHENG ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,10-12,14-16,19,20,35,39,46-48,53,60,66,67 and 70-76* is/are pending in the application.

4a) Of the above claim(s) *35,39,46-48,53,60 and 66* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,6,10-12,19,20,67,70,72,75 and 76* is/are allowed.

6)☒ Claim(s) *71 and 74* is/are rejected.

7)☒ Claim(s) *71 and 73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The three (3) NPL references cited on the IDS filed 5/25/07 lack dates in the citations. The references themselves have been considered, however, the citation is improper and is therefore unintialed by the examiner.

DETAILED ACTION

1. Applicant's amendment and response filed May 25, 2007 is acknowledged and entered. Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 35, 39, 46-48, 53, 60, 66, 67 and 70-76 are pending. Claims 35, 39, 46-48, 53, 60 and 66 are withdrawn from consideration being drawn to non-elected subject matter. Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 67 and 70-73 are under examination with respect to SEQ ID NO: 1, 9 and 10, respectively.

Response to Amendment/Arguments

2. The rejection of claims 1, 2, 4, 6, 10, 12, 14, 15, 16, 19, 20, 67 and 70-73 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, is withdrawn in view of Applicant's amendment clarifying the claim language.

The rejection of claims 1, 2, 4, 6, 10, 11, 12, 14, 15, 16, 19 and 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicant's persuasive arguments.

Claims Summary and Interpretation

3. The claims are drawn to an isolated or recombinant nucleic acid molecule (DNA, cDNA, RNA or an artificial nucleic acid) comprising a polynucleotide sequence selected from the group consisting of:

(a) the full length SEQ ID NO: 1 or the full-length complement thereof,

(b) a polynucleotide sequence greater than 97.8% identical to SEQ ID NO: 1 or the full-length complementary sequence thereof, wherein the polynucleotide sequence encodes an infectious, replicating respiratory syncytial virus, and,

(c) a polynucleotide sequence encoding an amino acid sequence or unique subsequence selected from the group consisting of an amino acid sequence greater than 99.5% identical to SEQ ID NO: 9, and an amino acid sequence greater than 96.4% identical to SEQ ID NO: 10, wherein an RSV that comprises the amino acid sequence is infectious and replicating.

Specifically, the nucleic acid molecule of (b) is at least 98.5% identical to SEQ ID NO: 1, or a complementary sequence thereof. In another embodiment, the nucleic acid molecule has at least one artificially mutated nucleotide, such as a deleted, inserted or substituted nucleotide. The mutation is located in the open reading frame encoding the polypeptide of SEQ ID NO: 10. Specifically the deletion in SEQ ID NO: 10 is a mutation of amino acid residue 1, 4, 10 or a combination thereof. In another embodiment, the open reading frame of SEQ ID NO: 10 is deleted.

Similarly, the polypeptide encoded by the polynucleotide of (c) comprises at least one deleted, inserted or substituted amino acid residue. The substitutions are listed in claim 11.

The unique polynucleotide subsequence of the polynucleotide of (c) comprises at least one complete ORF, such as SEQ ID NO: 9 and 10, or a plurality of complete ORFs.

Newly amended claim 67 is drawn to an isolated or recombinant nucleic acid comprising at least one unique polynucleotide subsequence comprising at least 500 contiguous nucleotides of SEQ ID NO: 1 or a complementary sequence thereof, with the proviso that the unique sequence includes at least one subsequence not included in SEQ ID NO: 14-19 or the full-length

complementary sequence thereof. More specifically, the subsequence comprises at least 1000 contiguous nucleotides of SEQ ID NO: 1. Also embodied is a subsequence that encodes at least 20, at least 50, at least 100, or at least 200 contiguous amino acid residues of SEQ ID NO: 9 or 10. Further, the subsequence encodes at least 50 contiguous amino acid residues of SEQ ID NO: 10. In another embodiment, the subsequence comprises at least one polynucleotide subsequence from a different strain of virus, or at least one polynucleotide subsequence from a different strain of human RSV, or at least one subsequence from a different species of virus.

Claim Objections

4. *(New Objection)* Claims 71 and 73 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is unclear how the unique polynucleotide subsequence of claim 67 (containing at least 500 contiguous nucleotides of SEQ ID NO: 1) is further limited by the limitation in claim 71, "wherein the unique polynucleotide subsequence encodes at least 20, at least 50, at least 100" amino acid residues of SEQ ID NO: 9 or 10. If the unique polynucleotide subsequence encodes at least 20, but not more than 20 amino acids of SEQ ID NO: 9 or 10, then the unique polynucleotide subsequence cannot also be comprised of at least 500 contiguous nucleotides of SEQ ID NO: 1. Further clarification is required as to how SEQ ID NO: 9 and 10 related to SEQ ID NO: 1. It appears that claim 71 fails to further limit claim 67. (Claim 73 is included in this objection as it depends from claim 71.)

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(New Rejection) ***Claim 74 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.***

Claim 74 recites, "wherein the isolated or recombinant nucleic acid comprises a polynucleotide sequence of SEQ ID NO: 1 or the complementary polynucleotide sequence thereof." It is unclear whether Applicant intends to claim a fragment of SEQ ID NO: 1, or the full-length SEQ ID NO: 1. If the full-length sequence is intended, then suggested language is, "wherein the isolated or recombinant nucleic acid comprises the polynucleotide sequence of SEQ ID NO: 1 or the complementary polynucleotide sequence thereof."

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(*New Rejection*) Claim 71 is rejected under 35 U.S.C. 102(b) as being anticipated by Karron et al. (PNAS USA, 1997, 94:13961-13966, "Karron"). The Office notes that claim 71 was previously rejected over the same reference, and that rejection was withdrawn. However, upon further consideration of the claimed subject matter in claim 71, the rejection is reinstated.

An explanation follows. Note that claim 67 is not rejected, although it is the parent claim of claim 71, because it appears that claim 71 fails to further limit claim 67.

Claim 71 is drawn to an isolated or recombinant nucleic acid comprising at least one unique polynucleotide subsequence, wherein the unique polynucleotide subsequence encodes at least 20, at least 50, at least 100 or at least 200 contiguous amino acid residues of SEQ ID NO: 9 or 10. The Office interprets the claim to read on any sequence that comprises at least 20 contiguous amino acid residues of SEQ ID NO: 9 or 10. Karron discloses a sequence comprising 171 contiguous amino acids that are identical to SEQ ID NO: 9 (aa 1-171), see alignment reproduced below.

```
RESULT 2
042050_HRSV
ID   042050_HRSV PRELIMINARY;      PRT;   195 AA.
AC   042050;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-FEB-2005 (TrEMBLrel. 29, Last annotation update)
DE   Matrix protein 2.
OS   Human respiratory syncytial virus.
OC   Viruses; ssRNA negative-strand viruses; Mononegavirales;
OC   Paramyxoviridae; Pneumovirinae; Pneumovirus.
OX   NCBI_TaxID=11250;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   STRAIN=B1;
RX   MEDLINE=98054343; PubMed=9391135; DOI=10.1073/pnas.94.25.13961;
RA   Karron R.A., Buonagurio D.A., Georgiu A.F., Whitehead S.S.,
RA   Adamus J.E., Clements-Mann M.L., Harris D.O., Randolph V.B.,
RA   Udem S.A., Murphy B.R., Sidhu M.S.;
RT   "Respiratory syncytial virus (RSV) SH and G proteins are not essential
RT   for viral replication in vitro: clinical evaluation and molecular
RT   characterization of a cold-passaged, attenuated RSV subgroup B
RT   mutant.";
RL   Proc. Natl. Acad. Sci. U.S.A. 94:13961-13966(1997).
DR   EMBL; AF013255; AAB82447.1; -; Genomic_RNA.
DR   EMBL; AF013254; AAB82437.1; -; Genomic_RNA.
DR   GO; GO:0019031; C:viral envelope; IEA.
DR   GO; GO:0003676; F:nucleic acid binding; IEA.
DR   GO; GO:0005198; F:structural molecule activity; IEA.
DR   GO; GO:0046782; P:regulation of viral transcription; IEA.
```

```
DR   InterPro; IPR009452; Pneumovirus_M2.
DR   InterPro; IPR000571; Znf_CCCH.
DR   Pfam; PF06436; Pneumovirus_M2; 1.
DR   Pfam; PF00642; zf-CCCH; 1.
KW   Matrix protein.
SQ   SEQUENCE   195 AA;  22309 MW;  BE231D88E00C2A01 CRC64;

  Query Match             99.4%;  Score 1007;  DB 2;  Length 195;
  Best Local Similarity   99.5%;  Pred. No. 2.7e-66;
  Matches  194;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MSRRNPCKFEIRGHCLNGRRCHYSHNYFEWPPHALLVRQNFMLNKILKSMDKSIDTLSEI 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSRRNPCKFEIRGHCLNGRRCHYSHNYFEWPPHALLVRQNFMLNKILKSMDKSIDTLSEI 60

Qy         61 SGAAELDRTEEYALGIVGVLESYIGSINNITKQSACVAMSKLLIEINSDDIKKLRDNEEP 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGAAELDRTEEYALGIVGVLESYIGSINNITKQSACVAMSKLLIEINSDDIKKLRDNEEP 120

Qy        121 NSPKIRVYNTVISYIESNRKNNKQTIHLLKRLPADVLKKTIKNTLDIHKSITISNPKEST 180
              |||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db        121 NSPKIRVYNTVISYIESNRKNNKQTIHLLKRLPADVLKKTIKNTLDIHKSIIISNPKEST 180

Qy        181 VNDQNDQTKNNDITG 195
              |||||||||||||||
Db        181 VNDQNDQTKNNDITG 195
```

Karron also discloses a sequence comprising 27 amino acids that are identical to amino acids 1-27 of SEQ ID NO: 10, see sequence alignment reproduced below.

```
RESULT 2
042047_HRSV
ID   042047_HRSV PRELIMINARY;      PRT;    90 AA.
AC   042047;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-FEB-2005 (TrEMBLrel. 29, Last annotation update)
DE   Matrix protein 2.
OS   Human respiratory syncytial virus.
OC   Viruses; ssRNA negative-strand viruses; Mononegavirales;
OC   Paramyxoviridae; Pneumovirinae; Pneumovirus.
OX   NCBI_TaxID=11250;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   STRAIN=B1;
RX   MEDLINE=98054343; PubMed=9391135; DOI=10.1073/pnas.94.25.13961;
RA   Karron R.A., Buonagurio D.A., Georgiu A.F., Whitehead S.S.,
RA   Adamus J.E., Clements-Mann M.L., Harris D.O., Randolph V.B.,
RA   Udem S.A., Murphy B.R., Sidhu M.S.;
RT   "Respiratory syncytial virus (RSV) SH and G proteins are not essential
RT   for viral replication in vitro: clinical evaluation and molecular
RT   characterization of a cold-passaged, attenuated RSV subgroup B
RT   mutant.";
RL   Proc. Natl. Acad. Sci. U.S.A. 94:13961-13966(1997).
```

```
DR   EMBL; AF013254; AAB82438.1; -; Genomic_RNA.
DR   EMBL; AF013255; AAB82448.1; -; Genomic_RNA.
DR   GO; GO:0005198; F:structural molecule activity; IEA.
DR   InterPro; IPR009969; Pneumo_M2.
DR   Pfam; PF07380; Pneumo_M2; 1.
KW   Matrix protein.
SQ   SEQUENCE   90 AA;  10587 MW;  16D886E983DE3994 CRC64;

  Query Match             92.0%;  Score 459;  DB 2;  Length 90;
  Best Local Similarity   94.4%;  Pred. No. 4.9e-40;
  Matches   85;  Conservative    3;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          4 MTKPKIMILPDKYPCSISSILISSESMVATFNHKNILQFNHNHLDNHQCLLNHIFDEIHW 63
              |||||||||||||||||||||||||||:||||||||||||||||||| |||:|||||||
Db          1 MTKPKIMILPDKYPCSISSILISSESMIATFNHKNILQFNHNHLDNHQRLLNNIFDEIHW 60

Qy         64 TPKNLLDTTQQFLQHLNIPEDIYTVYILVS 93
              ||||||| |||||||||||||||:|||||
Db         61 TPKNLLDATQQFLQHLNIPEDIYTIYILVS 90
```

Therefore, in view of the interpretation of the claim, the claimed subject matter is anticipated by the prior art.

Conclusion

7. Claims 1, 2, 4, 6, 10-12, 1416, 19, 20, 67, 70, 72, 75 and 76 are free of the prior art. This action is made non-final in view of the reinstatement of the 102(b) rejection over claim 71 in view of Karron.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 9-11-2007
Primary Examiner, TC1600